

**CLAIMS**

1. The combination of a growth hormone secretagogue and at least one agent which modifies the production or processing of A $\beta$  in the brain, said at least one agent being selected from:

- (a) compounds which inhibit the secretion of A $\beta$ ;
- (b) compounds which selectively inhibit the secretion of the 1-42 isoform of A $\beta$ ;
- (c) compounds which inhibit the aggregation of A $\beta$ ; and
- (d) antibodies which selectively bind to A $\beta$ ;

for use in treatment or prevention of a disease associated with deposition of A $\beta$  in the brain.

2. The use, for the manufacture of a medicament for treatment or prevention of a disease associated with deposition of A $\beta$  in the brain, of a growth hormone secretagogue and an amyloid modifier selected from:

- (a) compounds which inhibit the secretion of A $\beta$ ;
- (b) compounds which selectively inhibit the secretion of the 1-42 isoform of A $\beta$ ;
- (c) compounds which inhibit the aggregation of A $\beta$ .

3. Use according to claim 2 wherein the disease is Alzheimer's disease.

4. Use according to claim 3 wherein the medicament is for administration to a patient suffering from MCI.

5. Use according to claim 4 wherein the patient additionally possesses one or more risk factors for developing AD selected from: a family history of the disease; a genetic predisposition to the disease; elevated serum cholesterol; adult-onset

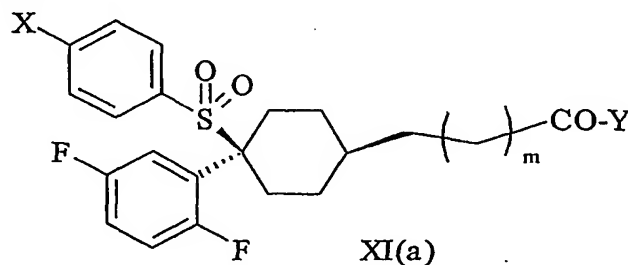
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diabetes mellitus; elevated baseline hippocampal volume; elevated CSF levels of total tau; elevated CSF levels of phospho-tau; and lowered CSF levels of A $\beta$ (1-42).

6. Use according to any of claims 2-5 wherein the growth hormone secretagogue is N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethoxy)ethyl]-2-amino-2-methylpropanamide, or pharmaceutically acceptable salt thereof.

7. Use according to any of claims 2-6 wherein the amyloid modifier is a  $\gamma$ -secretase inhibitor.

8. Use according to claim 7 wherein the  $\gamma$ -secretase inhibitor is a compound of formula XIa:



and the pharmaceutically acceptable salts thereof, wherein m is 0 or 1, X is Cl or CF<sub>3</sub>, and Y is OH, OC<sub>1-6</sub>alkyl, NH<sub>2</sub> or NHC<sub>1-6</sub>alkyl.

9. Use according to any of claims 2-6 wherein the amyloid modifier is a compound which selectively inhibits the secretion of the 1-42 isoform of A $\beta$ .

10. Use according to claim 9 wherein the amyloid modifier is R-flurbiprofen.

11. A pharmaceutical composition comprising in a pharmaceutically acceptable carrier, a growth hormone secretagogue and an amyloid modifier selected from:

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- (a) compounds which inhibit the secretion of A $\beta$ ;
- (b) compounds which selectively inhibit the secretion of the 1-42 isoform of A $\beta$ ; and
- (c) compounds which inhibit the aggregation of A $\beta$ .

12. A kit comprising a first medicament comprising a growth hormone secretagogue and a second medicament comprising an amyloid modifier selected from:

- (a) compounds which inhibit the secretion of A $\beta$ ;
- (b) compounds which selectively inhibit the secretion of the 1-42 isoform of A $\beta$ ;
- (c) compounds which inhibit the aggregation of A $\beta$ ; and
- (d) antibodies which selectively bind to A $\beta$ .

together with instructions for administering said medicaments sequentially or simultaneously to a patient suffering from AD, age-related cognitive decline, MCI, cerebral amyloid angiopathy, multi-infarct dementia, dementia pugilistica or Down syndrome.

13. A method of treatment or prevention of a disease associated with deposition of A $\beta$  in the brain comprising administering to a subject in need thereof a therapeutically effective amount of a growth hormone secretagogue (GHS) in combination with a therapeutically effective amount of at least one agent which modifies the production or processing of A $\beta$  in the brain, said at least one agent being selected from:

- (a) compounds which inhibit the secretion of A $\beta$ ;
- (b) compounds which selectively inhibit the secretion of the 1-42 isoform of A $\beta$ ;
- (c) compounds which inhibit the aggregation of A $\beta$ ; and
- (d) antibodies which selectively bind to A $\beta$ .